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Review

# A mini-review and perspective on multicyclic peptide mimics of antibodies

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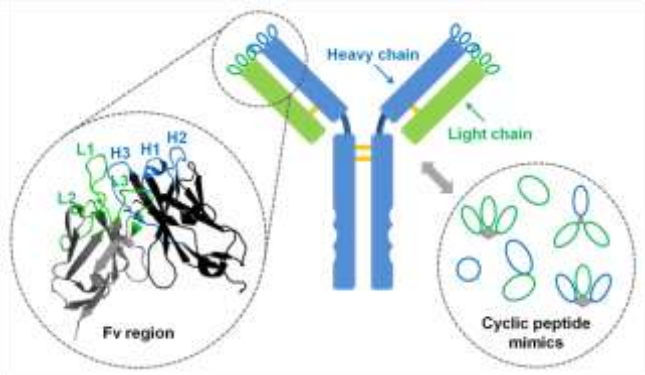
## Graphical Abstract




This review gives a brief introduction on recent development in monocyclic and multicyclic peptide mimics of antibodies and provides a perspective on screening and design of multicyclic peptide mimics of antibodies in the future.

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ABSTRACT

Affinity reagents are important tools in the biological sciences for understanding biological processes and for studying protein expression, localization and interactions. However, traditional affinity reagents such as antibodies (and their fragments) and non-immunoglobulin (non-Ig) scaffold binders, usually suffer from problems of poor cellular uptake efficiency, high production cost, low structural stability, and etc. This leads to rapid development of small antibody-like affinity reagents such as scaffold-free cyclic and multicyclic peptides, which usually have 5–30 amino acid residues, thus lying between non-Ig scaffolds and small molecules in size. In this mini-review, we highlight the recent development in mono-/multi-cyclic peptide mimics of antibodies, including cyclic peptide affinity reagents that have been developed for use in antibody-like applications, novel synthetic strategies for multicyclic peptides, and promising peptide library screening platforms. We also provide a perspective on the future development in multicyclic peptide mimics of antibodies.

## 1. Introduction

Antibodies are among the most commonly used and most important tools in the biological sciences for understanding biological processes and studying protein expression, localization and interactions. However, they are also among the most common causes of problems in biological experiments due to the difficulty in sourcing validated and batch-to-batch reproducible antibodies [1, 2]. Among two million antibodies on the market, up to half of them are probably unreliable in recognizing the right targets [2, 3]. Moreover, the use of antibodies (including also the antibody fragments) inside living cells are limited owing to their poor efficiency of cellular uptake and their instability in reducing environments of the cytoplasm; in

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